enemata than by the exhibition of the opiate by the mouth. I cannot but believe that not only is the system brought under its influence, but that a local anæsthesia is thus speedily induced, which is of itself of great benefit.[1] Were another case of chorea with pregnancy to present itself to me, I should, after the bowels had been moved by gentle laxatives (not by drastic purges, which are themselves irritants), resort to injections of laudanum, repeated sufficiently often to keep the system under their influence, and continued until the system had become accustomed to the cause of the irritation, or the diseased habit overcome. Of course the existence of great cerebral congestion would contraindicate the free use of opium, while, on the other hand, this treatment need not interfere with the exhibition of medicines likely to improve the general tone of the system, the preparations of iron or other tonics.

PHILADELPHIA, February 13, 1861.

ART. III.—*On the Antagonistic Effects of Opium and the Mydriatics, Illustrated by Cases of Poisoning in the Human Subject.* By CHAS. CARROLL LEE, M. D., Resident Physician to the Pennsylvania Hospital.

ON the 3d of September, 1861, three well-marked cases of poisoning by stramonium seeds were admitted to the Pennsylvania Hospital. One was a man, aged 31, the other two were women, aged respectively 34 and 58 years.

The history of the accident was as follows: The two women were about moving into a new house, and the man was assisting them with their furniture, when, in passing an unoccupied room, he saw in an open closet a bottle filled with what he supposed to be brandy. He poured out a cupful, drank it, and offered some to the women, who both drank of it—the elder about a gill, and the younger only one or two mouthfuls. A child of the latter was also given a little of the mixture, and it was in this case that the effects of the poison were first noticed. Within four or five minutes after taking the draught, the child became violently flushed in the face, the eyes glittered and rolled about, and it tottered so as almost to fall from its chair. This alarmed the mother, who at once supposed they had taken poison, and, though already giddy and half blind, she managed to run with the bottle to a neighbouring druggist, who confirmed her suspicions. With much difficulty she again reached her house, where she found the other woman and the man lying speechless on the floor; and, as their friends who crowded around them could afford no assistance, the three were put into a wagon, and driven without further delay to the hospital.

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[1] One reason why enemata of laudanum are not more relied on in the treatment of disease, is the fact that, as usually given, the amount of liquid (f℥ij of starch water) is too large to be retained. Excepting in cases of rectal inflammation, it is much better to use but *half an ounce of tepid water*, which is rarely rejected, and acts promptly.

The bottle, which contained a number of small, black, kidney-shaped seeds, and a little whiskey, was brought with them, and, as soon as examined, the seeds were pronounced *stramonium.* This was confirmed by the appearance of the patients, which was very striking.

The man and the elder woman were nearly comatose, their faces flushed to an almost violet hue, the conjunctivæ injected, and the pupils were insensible to light, and so strongly dilated, as to leave visible merely a rim of iris; the skin of the face and upper extremities was burning hot, the tongue and throat parched and dry, respiration slow and laboured, pulse 100, and very tense and full.

The younger woman had taken a smaller dose of the poison than the others, and had reached only the maniacal stage of its influence; the skin was scarlet and burning hot, and the mydriasis as marked as in the other cases, the tongue parched, intense thirst, but no constriction of the fauces on swallowing; the respiration, however, was hurried, the pulse fluttering, and beating 140 to the minute. The patient was violently delirious, resembling, in a marked degree, the most excited stage of *delirium tremens,* struggling to get out of bed, and continually rolling from side to side; she was unable to stand by herself, and, unless supported, fell forward to the ground. When her hands were not restrained, it was observed that she pursued imaginary objects in the air, or picked at the bedclothes, as in the delirium of typhoid fever. No frothing at the mouth, or relaxation of the sphincters, said by Taylor to characterize poisoning by stramonium and belladonna, occurred.

Treatment.—As neither of the women had vomited since drinking the poison, I first resorted to the stomach-pump, which, with the assistance of my colleagues, was used freely. About a pint of thin, dark-brownish liquid was pumped up, and carefully examined, but contained no seeds. The stomach was then washed out with tepid water, but no seeds were obtained. The symptoms being in all respects similar to those of poisoning by belladonna, an antidote to that narcotic, on which I place entire reliance, was next administered, viz.: *Opium* in doses sufficient to secure a full opiate impression, as indicated by contraction of the pupil. Forty drops of laudanum were immediately ordered to each of the women, and having at hand some of Magendie's Solution of Morphia—in this hospital only used for hypodermic injections—I gave them fifteen minims apiece, holding in solution a half grain of the salt, every half hour, until each had taken two grains.

As considerable debility had been induced by their struggles when the stomach-tube was used, a half ounce of brandy was added to each dose of the morphia; this was deemed the more necessary because, notwithstanding the well-known stimulating effect of stramonium in the first stage, this period had already passed. The result justified our expectations; for in two hours the pulse of the younger woman had fallen to 90 beats per minute. This patient was now nearly well, and the other woman in a fair way of recovery; the morphia was therefore diminished to a quarter of a grain every hour, with an ounce of wine instead of brandy; this was continued through the night, and the following day the women were discharged from the hospital cured.

The man exhibited much the same symptoms as the women, catching and striking at imaginary objects around him, but the retina was insensible to light, for a hand passed close in front of the eye failed to make him wink, unless the cornea was touched; he was also more comatose at first, and with a more feeble and rapid pulse—150 per minute. Another alarming symptom was an apparent somnolency, which, according to some authors, marks only the worst cases. Thus, Dr. Stillé says: "At no period in the progress of the symptoms, *until death grows imminent*, is there the least tendency to sleep; on the contrary, there is an obstinate insomnia; and yet, on the recovery of the patient, he retains no distinct recollection of what has occurred."[1]

Before leaving home he had been given two or three emetics, which had acted very freely; the stomach-pump was therefore not used, and he was at once ordered forty drops of laudanum, to be repeated in ten minutes, after which he was given a half grain of muriate of morphia every half hour, until three and a half grains of the salt had been taken—a larger amount than in the other cases, as he had imbibed a much larger dose of the poison; this, with ice to the head, constituted his entire treatment. He rallied during the night, slept a little, and the next morning was able to walk, and read large type. Some abnormal dilatation of the pupil and vertigo remained, however, during the day; by evening he was quite well.

The effect of the morphia was equally evident in each of the foregoing cases. They had been brought to the hospital and subjected to treatment about an hour and a half after the poison was swallowed; within an hour after the first administration of the antidote—for such, I think, it may justly be considered—a decided amelioration of all the symptoms, especially of the mydriasis, was perceptible; while in three hours, the mildest case was quite well, and the other two so much improved as to excite no further uneasiness. That this improvement was not due merely to the stomach-pump or emetics is apparent, from the fact that the man, who had vomited profusely, presented the most alarming symptoms of debility and coma; while in the case of both the women, the fluid obtained through the stomach-tube resembled rather the ordinary contents of the stomach than the stramonium mixture.

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[1] Therapeutics and Mat. Med., ii. 55.

There was every probability, indeed, that the small amount swallowed—and the concentrated strength of the mixture may be inferred from its effects—had been absorbed before the evacuants were used.

As corroborative of the results obtained in the preceding cases, and as further illustrative of the *mutual antagonistic influence* of opium and belladonna, a brief description of two other cases that occurred to me while Resident Physician in the Philadelphia Hospital, Blockley, may not prove uninteresting.

The first, a child, aged six years, had been given, in mistake for syrup of rhubarb, a drachm of *succus belladonnæ*, an unofficinal preparation, very concentrated, and only used in collyria. The characteristic symptoms of belladonna poisoning were almost immediately apparent; the child's face became scarlet, and it tottered and fell insensible to the floor. I was instantly sent for, and found the flush on the face deepening to a violet hue, the eyes fixed and staring, the pupils dilated to the utmost, tongue dry, pulse slow and bounding, and the child almost comatose. No stomach-pump was at hand, and I at once resolved to test the effect of opium. Twenty drops of laudanum by the mouth, and the same amount by the rectum, were simultaneously given, and at intervals of a half hour the dose of twenty drops was repeated, until the little patient had taken 120 drops in all. After the third dose the pupils began strongly to contract, the purple hue of face to fade, and in three hours the child was well, and running about the room.

The second case alluded to was, on the contrary, one of opium poisoning, occurring in a child aged two years. The quantity of laudanum taken could not be ascertained, for the mother who had given the drug (as was supposed for the purpose of infanticide), obstinately refused to answer any question on the subject.

Enough, however, had been swallowed to render a fatal prognosis almost positive. The skin was pale, cold, and clammy, pulse feeble, and beating only forty to the minute, respiration slow and laborious, pupils excessively contracted, and coma profound. A galvanic battery was sent for, but when obtained, was so out of order as to be useless.

Some tincture of belladonna, however, was at hand, and was instantly given in doses of fifteen minims, repeated at intervals of twenty minutes, until four doses were taken. The first perceptible change was after the second dose, when the temperature of the skin rose several degrees; this was gradual, but was distinctly felt by the hand.

A few minutes after the third dose of belladonna the eyes were carefully examined, and the pupils, although still contracted, were no longer insensible to light; the skin was much warmer, and a faint blush appeared on the face and neck; respiration twenty-five, pulse eighty-six per minute. When spoken to, the child now opened its eyes, and showed signs of intelligence; but, as some drowsiness yet remained, the fourth and last dose of belladonna was given, at the same interval as before. Its effect was rather more rapid and striking than was desired; for in a few minutes after taking it, the child's face, neck, and arms became flushed as red as in the scarlatinal eruption, and the pupils dilated much beyond their proper size. The child started up in bed, shouted and laughed immoderately, and, in fact, exhibited every sign of the first stage of belladonna intoxication. Not wishing to substitute one poison for another, I now stopped the belladonna, and in less than an hour the scarlet blush was imperceptible, the pupils contracted and dilated regularly, and the child was to all appearances well; no vomiting or other disagreeable sequela occurred.

These two cases were typical ones of their kind. They were both strongly marked—the first dangerous, the latter almost hopeless; in both the antidotal effects of opium and belladonna were fairly and honestly tested; and, although a general conclusion cannot be drawn from isolated cases, a careful consideration of the phenomena will warrant the inference —1st, that the poisonous symptoms were promptly subdued by the remedy administered; and, 2d, that the antidote was safely given in doses which would have been surely fatal in health.

The knowledge of the antidotal powers of belladonna in cases of opium poisoning is not of very recent date. Dr. Graves first suggested that, in continued fever, with coma and contracted pupils, if an agent could be found to overcome the latter symptom, it might also relieve the other signs of cerebral derangement; and for several years past, cases analogous to the preceding have been reported in the journals. The first paper bearing directly on this point, with which I am acquainted, was read by Dr. Thos. Anderson, before the Physiological Society of Edinburgh, in Jan. 1854. He relates two well-marked cases of poisoning; the first by an overdose of muriate of morphia, which was cured by six drachms of tincture of belladonna. The second, an elderly woman, had taken five drachms of laudanum for self-destruction. The stomach-pump, electricity, and other measures were tried without effect, when Dr. Anderson resolved to administer the tincture of belladonna. He gave an ounce on the spot, and within the next half hour two drachms more. In five hours, all indications of opium poisoning had disappeared.[1]

Again, Dr. Mussey, of Cincinnati, reports a case of poisoning by an ounce of laudanum, in which, five hours after it had been swallowed, he gave first the extract, then the tincture of belladonna, until seven grains of the former, and one ounce of the latter were taken. Recovery was prompt and complete, without any of the peculiar effects of belladonna, except indistinct vision for a few hours.[2]

On the other hand, Mr. Bell, of Edinburgh, records two cases in which large quantities of morphia quickly subdued alarming symptoms of poisoning by hypodermic injections of atropia;[1] and I may add that, within the last six months, two others, precisely similar, have come under my notice, in this Hospital. In these, the poisonous impression was produced by injecting respectively the one-thirtieth and the one-thirty-fifth of a grain of sulphate of atropia.

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[1] Monthly Journal of Med. Sciences, April, 1854.

[2] Boston Med. and Surg. Journal, February, 1856.

Mr. Seaton, of Leeds, has related the history of ten persons who were poisoned by the berries of the atropa belladonna. In two of these cases the effects were slight, and required only an emetic. In the other eight the symptoms were alarming and well marked, especially wakefulness and active delirium. Opium was given to all; and in seven of the worst cases, the symptoms disappeared as soon as sleep and contraction of the pupil indicated its influence on the system. The eighth patient, who was a scrofulous woman, long out of health, took but little opium, and died.[2] In the *London Medical Review*, for August, 1860, there is a most interesting paper on the Significance of the Effects of Opium and Belladonna on the Pupil, by Richard Hughes, Esq., of Brighton. He discusses with much ability the relative and antagonistic effects of the pure narcotics and the mydriatics, and adduces numerous cases corroborative of the foregoing.

Dr. Lopez, of Mobile, describes the case of an apothecary, at the Marine Hospital, who poisoned himself by the application of a large belladonna plaster to the knee, after the cuticle had been removed; there existed nausea, giddiness, mydriasis, and extreme prostration. Having frequently tested the reciprocal influence of opium and belladonna, Dr. Lopez at once prescribed a drachm of laudanum, to be followed by fifteen drops every half hour until the symptoms abated. The first dose sufficed to antagonize the belladonna in thirty minutes.[3]

M. Brown-Séquard, while admitting that belladonna and opium have some properties diametrically opposed—thus, for instance, belladonna contracts the vessels of the spinal marrow, and opium, like strychnia, paralyzes them—says that in animals poisoned by opium, belladonna excited no influence, that he could observe, on the fatal symptoms. He further alludes to a case of poisoning by opium and belladonna taken simultaneously, and infers that their employment as mutual antidotes is nugatory.[4]

But unfortunately for these objections, no correct conclusion can be drawn from experiments made on the lower animals, as they are variously affected by narcotics. Thus, Dr. Anderson has given to cats and dogs enormous doses of morphia, without producing any appreciable effect; and to them five and six grains of atropia proved quite harmless. Rabbits will feed for months on belladonna leaves and have their pupils dilated all the time, but otherwise they are not affected. Blackbirds eat belladonna berries in large quantities, and do not die. It is, therefore, only to experiments on man that any value can be attached.[1] As no description is given by M. Brown-Séquard, of his last-mentioned case, it is impossible to accord it due weight in the scale; for aught we know, a large amount of opium and a small quantity of belladonna, or *vice versâ*, may have been taken.

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[1] Edinburgh Med. Journal, July, 1858.

[2] Med. Times and Gaz., Dec. 3, 1859.

[3] North Amer. Med.-Chir. Rev., Jan. 1860.

[4] Journal de Physiologie, Oct. 1860, p. 726.

In commenting on the influence of belladonna in the various forms of paraplegia, the same author denies that it is a stimulant to the nerve centres, and remarks as follows: "We will not speak here of its action on the brain: but as regards the spinal cord and spinal nerves, belladonna, far from being a stimulant, acts in diminishing the vital properties of these organs. As we have already said, belladonna is a powerful excitant of the bloodvessels, and especially of those of the spinal cord and its membranes. In consequence of this influence it diminishes the amount of blood in the vertebral canal, and, in so doing, produces a relative diminution of the vital properties of the spinal cord and its nerves. It is, therefore, in those cases, in which these vital properties are increased, that belladonna should be employed."[2]

Without at all calling in question M. Brown-Séquard's views on the physiological effect of belladonna, which, we must take for granted, are based upon accurate experimentation, I think the cases I have already adduced (and others might be presented by the dozen were it necessary) are sufficient to establish an undeniable antagonism between opium and belladonna. To what extent this antagonism exists, or whether its ground is the vascular rather than the nervous system, are points that I am neither prepared nor inclined to discuss. In his work on Epilepsy, as well as in the extract just given, M. Brown-Séquard has stated contraction of the capillaries to be the uniform effect of the internal administration of belladonna; and Mr. Wharton Jones, in his Prize Essay on Inflammation, finds that the application of a solution of sulphate of atropia to the small arteries causes constriction of their calibre, while opium largely and at once dilates them; yet no one can doubt that this is through their influence on the sympathetic, which is the motor nerve of the bloodvessels.

Our knowledge of the ultimate effects of medicines is, however, still in its infancy, and well aware that even acute and experienced observers are apt to stumble in this field of inquiry, I have endeavoured to confine myself strictly to facts. These may, perhaps, have been misinterpreted throughout; but I have presented them for what they are worth, in the hope that they may contribute, in some degree, to illustrate so important a subject as the toxicology of the narcotics.

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[1] Edinburgh Med. Journ., June, 1860, p. 1100.

[2] Lancet, December 22, 1860, p. 605.

[3] Guy's Hospital Reports for 1850, pp. 8, 9.